

Virus Replication

John Goulding, Imperial College London, UK



As viruses are obligate intracellular pathogens they cannot replicate without the machinery and metabolism of a host cell. Although the replicative life cycle of viruses differs greatly between species and category of virus, there are six basic stages that are essential for viral replication.

1. Attachment: Viral proteins on the capsid or phospholipid envelope interact with specific receptors on the host cellular surface. This specificity determines the host range (**tropism**) of a virus.

2. Penetration: The process of attachment to a specific receptor can induce conformational changes in viral capsid proteins, or the lipid envelope, that results in the fusion of viral and cellular membranes. Some DNA viruses can also enter the host cell through receptor-mediated endocytosis.

3. Uncoating: The viral capsid is removed and degraded by viral enzymes or host enzymes releasing the viral genomic nucleic acid.

4. Replication: After the viral genome has been uncoated, transcription or translation of the viral genome is initiated. It is this stage of viral replication that differs greatly between DNA and RNA viruses and viruses with opposite nucleic acid polarity. This process culminates in the *de novo* synthesis of viral proteins and genome.

5. Assembly: After *de novo* synthesis of viral genome and proteins, which can be post-transcriptionally modified, viral proteins are packaged with newly replicated viral genome into new virions that are ready for release from the host cell. This process can also be referred to as maturation.

6. Virion release: There are two methods of viral release: **lysis** or **budding**. Lysis results in the death of an infected host cell, these types of viruses are referred to as **cytolytic**. An example is *variola major* also known as smallpox. Enveloped viruses, such as influenza A virus, are typically released from the host cell by budding. It is this process that results in the acquisition of the viral phospholipid envelope. These types of virus do not usually kill the infected cell and are termed **cytopathic viruses**.

After virion release some viral proteins remain within the host's cell membrane, which acts as potential targets for circulating antibodies. Residual viral proteins that remain within the cytoplasm of the host cell can be processed and presented at the cell surface on MHC class-I molecules, where they are recognised by T cells.

